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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/785,657	02/20/2001	Ulf Landegren	LANDEGREN=1A	5356

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EXAMINER	
CHUNDURU, SURYAPRABHA	
ART UNIT	**PAPER NUMBER**
1637	18

DATE MAILED: 10/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/785,657	LANDEGREN ET AL.	
	Examiner	Art Unit	
	Suryaprabha Chunduru	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-7,13-15 and 17-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-7,13-15 and 17-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicants' response to the office action (Paper No. 17) filed on May 27, 2003 has been entered.

Response to Arguments

2. Applicant's response to the office action (Paper No.17) is fully considered and deemed persuasive.

3. The rejection made under 35 U.S.C. 112 second paragraph in the previous office action is withdrawn herein in view of the applicants' amendment (Paper No.14).

New Grounds of Rejections

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 2-5, 7, and 19-20, 22-25 are rejected under 35 U.S.C. 102(e) as being anticipated by Landegren (USPN. 6,558,928).

Landegren teaches a method of claim 25, and 22, for detecting one or more analytes in a solution comprising (a) binding two or more proximity probes (first affinity probe, second affinity probe and padlock probe) to a respective binding site on said one or more analytes (polyepitopic target) not immobilized on a solid support (see column 4, lines 50-51), wherein the proximity probes comprise binding moiety (polynucleotide chain) with affinity for said analyte(s) and nucleic acids (polynucleotide sequence) acting as a reactive functionality coupled thereto (see column 6, lines 65-67, column 7, lines 1-20); (b) allowing the binding moiety to bind to one or more analytes and allowing the close proximity nucleic acids to interact with each other (see column 7, lines 21-27); (c) and detecting the degree of interaction between the nucleic acids (see column 7, lines 35-48); two or more proximity probes comprise a first proximity probe with a 3' free nucleic acid and the second proximity probe has a 5'free nucleic acid and a third proximity probe with 3' and 5' free nucleic acids wherein the 3, and 5' free nucleic acids of third probe interacts with 5' of the first proximity probe and 3' of the second proximity probe (see column 7, lines 10-27).

With regard to claim 2-5, and 7, 19-24, Landegren also teaches tat the method comprises (i) amplification of interacted nucleic acids and quantitation (concentration) of the amplified product (see column 7, lines 21-27, and lines 35-48); proximity probes are selected from polyclonal, monoclonal antibodies and fragments thereof , receptors, lectins (proteins and peptides) and nucleic acid aptamers (see column 7, lines 30-34); analyte is selected from nucleic acids (see column 2, lines 51-52); binding moieties of the proximity probe are on the same

analyte (see column 7, lines 21-27); nucleic acids are coupled to the binding moieties through splint template (padlock probe) and ligation of the nucleic acid ends (see column 7, lines 21-27). Thus the disclosure of Landegren meets the limitations in the instant claims

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

A. Claims 6, 13-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Landegren (USPN. 6,558,928) ('928) and in view of Landegren (WO 97/00446) (00446).

Landegren ('928) teaches a method of claim 6, and 13-15, for detecting one or more analytes in a solution comprising (a) binding two or more proximity probes (first affinity probe, second affinity probe and padlock probe) to a respective binding site on said one or more analytes (polyepitopic target) not immobilized on a solid support (see column 4, lines 50-51), wherein the proximity probes comprise binding moiety (polynucleotide chain) with affinity for

said analyte(s) and nucleic acids (polynucleotide sequence) acting as a reactive functionality coupled thereto (see column 6, lines 65-67, column 7, lines 1-20); (b) allowing the binding moiety to bind to one or more analytes and allowing the close proximity nucleic acids to interact with each other (see column 7, lines 21-27); (c) and detecting the degree of interaction between the nucleic acids (see column 7, lines 35-48); two or more proximity probes comprise a first proximity probe with a 3' free nucleic acid and the second proximity probe has a 5'free nucleic acid and a third proximity probe with 3' and 5' free nucleic acids wherein the 3, and 5' free nucleic acids of third probe interacts with 5' of the first proximity probe and 3' of the second proximity probe (see column 7, lines 10-27).

Landegren ('928) also teaches tat the method comprises (i) amplification of interacted nucleic acids and quantitation (concentration) of the amplified product (see column 7, lines 21-27, and lines 35-48); proximity probes are selected from polyclonal, monoclonal antibodies and fragments thereof , receptors, lectins (proteins and peptides) and nucleic acid aptamers (see column 7, lines 30-34); analyte is selected from nucleic acids (see column 2, lines 51-52); binding moieties of the proximity probe are on the same analyte (see column 7, lines 21-27); nucleic acids are coupled to the binding moieties through splint template (padlock probe) and ligation of the nucleic acid ends (see column 7, lines 21-27) . However, Landgren ('928) did not teach specifically binding moieties as antibodies and directed against the Fc portion of the further antibody, screening for ligand-receptor interation antagonists, detection of infectious agents in food and detection of a sample as a decrease in signal.

Landgren ('00446) teaches a method for detecting analyte(s) in a solution, wherein the method comprises binding of two or more proximity probes (oligonucleotides) to a respective

binding site on the analyte, wherein binding moieties comprise antibodies allowing binding moiety to bind to the analyte (antibody-antigen) and the proximity antibodies interact with each other and detecting the interaction between nucleic acids (oligonucleotides) (see page 1, abstract, page 3, paragraph 4, page 4, lines 1-8, 21-31). Landgren also teaches that the method comprises (i) amplification of the interacted nucleic acids and detection of amplified product (see page 4, lines 7-8,); binding moieties of the proximity probes selected from antibodies, lectin, receptors, nucleic acids (oligonucleotides) (see page 4, paragraph 5, and page 5, paragraph 5); detection of an unknown analyte in a solution, and screening ligand candidates (antibody-affinity reagents) (see page 6, paragraphs 1-3).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to combine a method for detecting one or more analytes as taught by Landegren ('928) with a method using antibody binding moieties, to achieve expected advantage of developing an improved method for detecting a target analyte using immunological reactants because Landegren ('00446). suggests that "his invention enables detection of extremely low numbers of antigenic molecules, even down to a single molecule (see page 3, paragraph 1). An ordinary practitioner would have been motivated to combine the teaching of Landegren ('928) with the teachings of Landegren ('00446) because incorporating the use of antibody binding moieties as taught by Landegren (00446) would increase the specificity by reducing the background signals due to interference of non-specific binding and enhance the signal of the amplification product which in turn enhance the detection of a target analyte.

B. Claims 17-18, and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Landegren (USPN. 6,558,928) ('928) and in view of Landegren et al. (USPN. 4,988,617) ('617).

Landegren ('928) teaches a method of claims 17-18, and 21, for detecting one or more analytes in a solution comprising (a) binding two or more proximity probes (first affinity probe, second affinity probe and padlock probe) to a respective binding site on said one or more analytes (polyepitopic target) not immobilized on a solid support (see column 4, lines 50-51), wherein the proximity probes comprise binding moiety (polynucleotide chain) with affinity for said analyte(s) and nucleic acids (polynucleotide sequence) acting as a reactive functionality coupled thereto (see column 6, lines 65-67, column 7, lines 1-20); (b) allowing the binding moiety to bind to one or more analytes and allowing the close proximity nucleic acids to interact with each other (see column 7, lines 21-27); (c) and detecting the degree of interaction between the nucleic acids (see column 7, lines 35-48); two or more proximity probes comprise a first proximity probe with a 3' free nucleic acid and the second proximity probe has a 5'free nucleic acid and a third proximity probe with 3' and 5' free nucleic acids wherein the 3, and 5' free nucleic acids of third probe interacts with 5' of the first proximity probe and 3' of the second proximity probe (see column 7, lines 10-27).

Landegren ('928) also teaches tat the method comprises (i) amplification of interacted nucleic acids and quantitation (concentration) of the amplified product (see column 7, lines 21-27, and lines 35-48); proximity probes are selected from polyclonal, monoclonal antibodies and fragments thereof , receptors, lectins (proteins and peptides) and nucleic acid aptamers (see column 7, lines 30-34); analyte is selected from nucleic acids (see column 2, lines 51-52); binding moieties of the proximity probe are on the same analyte (see column 7, lines 21-27);

nucleic acids are coupled to the binding moieties through splint template (padlock probe) and ligation of the nucleic acid ends (see column 7, lines 21-27) . However, Landgren ('928) did not teach specifically binding moieties as antibodies and directed against the Fc portion of the further antibody, screening for ligand-receptor interation antagonists, detection of infectious agents in food and detection of a sample as a decrease in signal.

Landegren et al. (USPN. 4,988,617).

Landgren et al. teach a method for detecting analyte(s) (target nucleic acid) in a solution, wherein the method comprises binding of two or more proximity probes (oligonucleotides) to a respective binding site on the analyte, wherein the proximity probes are comprised of a binding moiety (biotin) and allowing binding moiety to bind to the analyte and the proximity probes interact with each other (adjacent oligonucleotide probes join each other) and detecting the interaction between nucleic acids (oligonucleotides) (see column 3, lines 1-38, column 4, lines 34-50, column 10, 48-60). Landgren et al. also teach that the method (i) comprises binding moieties of the proximity probes selected from antibodies, carbohydrate and complementary strands of DNA (see column 10, lines 60-67); (ii) can be used to detect infectious agents in a test substance (see column 4, lines 12-19); no signal is observed to a linked probe product which would be formed if the target analyte were present (see column 16, lines 35-39).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to combine a method for detecting one or more analytes as taught by Landegren ('928) with a method using different binding moieties, to achieve expected advantage of developing an improved method for detecting a target analyte using labeled moieties because Landegren (''617). suggests that "fluorescent detection permits

multicolor analysis whereby the presence of alternate alleles or a quantitative comparison of two genes can be analyzed in an internally controlled fashion (see column 8, lines 66-68, column 9, lines 1-2). An ordinary practitioner would have been motivated to combine the teaching of Landegren ('928) with the teachings of Landegren (''617) because incorporating the use of labeled binding moieties as taught by Landegren ('617) would increase the specificity by increased detection of specific binding and enhance the detection of a target analyte.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 703-305-1004. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Suryaprabha Chunduru
October 7, 2003

JEFFREY FREDMAN
PRIMARY EXAMINER